AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A computer comprising a processor in communication with a memory; said memory having stored therein

(i) at least one set of x, y, and z atomic coordinates from Table 5, or a mathematical modification of Table 5 that preserves the relative relationships among the coordinates of Table 5, ~~or surrogate coordinate thereof, from Table 5 for~~ from a given atom of each of ~~the following~~ residues: His-538, Lys-540, Trp-414, and Leu-491 of a Polo-box domain of a Plk-1 Polo-like kinase, or a set of x, y, and z atomic coordinates that have a root mean square deviation of said set of x, y, and z atomic coordinates of said Polo-box domain of less than 3 Å ~~encoded on a data-storage medium~~; and

(ii) a program for generating a three-dimensional model of said Polo-box domain of said Plk-1 Polo-like kinase utilizing said coordinates of (i), above,

wherein said computer is capable of outputting a representation of said three-dimensional model of said Polo-box domain of said Plk-1 Polo-like kinase to a display or memory.

2. (Withdrawn) A computer comprising a processor in communication with a memory; said memory having stored therein a pharmacophore model of a phosphopeptide that binds a Polo-box domain and a program for displaying said model, said model comprising at least one of the following:

(i) a phosphate group on threonine that participates in at least 1 hydrogen-bonding interaction; and

(ii) a serine at the pThr-1 position, wherein the Ser-1 side chain is directed towards the Plk1 surface.

3. (Withdrawn) A method of selecting or designing a candidate ligand for a Polo-box domain, said method comprising the steps of:

(a) generating a three-dimensional structure of a Polo-box domain having at least one atomic coordinate, or surrogate thereof, from Table 5 for each of the following residues: His-538, Lys-540, Trp-414, or Leu-491or atomic coordinates that have a root mean square deviation from said coordinates of less than 3 Å; and

(b) selecting or designing a candidate ligand having sufficient surface complementary to said structure to bind a Polo-box domain in an aqueous solution.

4. (Withdrawn) A crystal of a Polo-like kinase complex comprising a Polo-box domain bound to a phosphopeptide complex.

5. (Withdrawn) The crystal of claim 4, wherein said Polo-like kinase is Plk-1.

6. (Withdrawn) The crystal of claim 4, wherein said Plk-1 comprises at least amino acids 326-603.

7. (Withdrawn) The crystal of claim 4, wherein said phosphopeptide comprises the amino acid sequence [Pro/Phe]-[ϕ/Pro]-[ϕ/Ala_{Cdc5p}/Gln_{Plk2}]-[Thr/Gln/His/Met]-Ser-[pThr/pSer]-[Pro/X], where ϕ represents hydrophobic amino acids.

8. (Withdrawn) The crystal of claim 4, wherein said phosphopeptide comprises the amino acid sequence MAGPMQ-S-**pT**-P-LNGAKK.

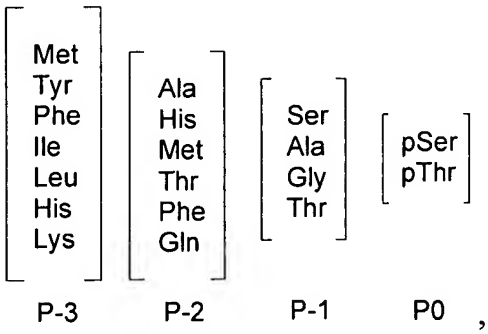
9. (Withdrawn) An isolated, less than full-length fragment of Polo-box domain comprising residues 367-603 of human Plk-1 Polo-box domain) in complex with a phosphopeptide comprising S-[pS/pT]-P/X, wherein X is any amino acid.

10. (Withdrawn) A phosphopeptide comprising the amino acid sequence

[Pro/Phe]-[ϕ/Pro]-[ϕ/Ala_{Cdc5p}/Gln_{Plk2}]-[Thr/Gln/His/Met]-Ser-[pThr/pSer]-[Pro/X], where ϕ represents hydrophobic amino acids.

11. (Withdrawn) The phosphopeptide of claim 10, comprising Pro-Met-Gln-Ser-pThr-Pro-Leu, wherein said phosphopeptide binds human Plk-1.

12. (Withdrawn) A phosphopeptide comprising the amino acid sequence,



wherein pSer and pThr are phosphorylated serine and phosphorylated threonine, and wherein the amino acids designated in P-3, P-2, or P1 may be natural or unnatural amino acids.

13. (Withdrawn) A method for treating or inhibiting a cellular proliferative disorder in a patient, said method comprising administering a pharmaceutical composition of the phosphopeptide of claim 10, wherein said phosphopeptide is in an amount sufficient to treat or inhibit the cellular proliferative disorder in said patient.

14. - 16. (Cancelled)

17. (Withdrawn) A method for identifying a peptidomimetic compound that modulates Polo-like kinase biological activity, said method comprising the steps of:

a) contacting the phosphopeptide of claim 1 and a Polo-box domain (PBD) polypeptide to form a complex between said phosphopeptide and said PBD;

b) contacting said complex with a candidate compound; and

c) measuring the displacement of said phosphopeptide from said PBD,

wherein said displacement of said phosphopeptide from said PBD indicates that said candidate compound is a peptidomimetic compound that modulates Polo-like kinase biological activity.

18. (Withdrawn) A method for identifying a peptidomimetic compound that modulates Polo-like kinase biological activity, said method comprising the steps of:

a) contacting the phosphopeptide of claim 1 and a PBD in the presence of a candidate compound; and

b) measuring binding of said phosphopeptide and said PBD,

wherein a reduction in the amount of binding relative to the amount of binding of said phosphopeptide and said polypeptide in the absence of said candidate compound indicates that said candidate compound is a peptidomimetic compound that modulates Polo-like kinase biological activity.

19. (Withdrawn) A method for identifying a binding pair consisting of a peptide and a peptide-binding domain comprising the steps of:

a) providing a biased peptide library comprising a collection of peptides fixed to a solid support, each peptide having at least two known amino acid residues whose position is invariant;

b) providing a pooled cDNA library, wherein the cDNA library is positioned for protein expression;

c) expressing the pooled cDNA library in the presence of a detectable label;

d) contacting the peptide library and the expressed cDNA library; and

e) detecting a peptide and peptide-binding domain interaction, wherein an interaction identifies a peptide and peptide-binding domain binding pair.

20. (Withdrawn) A method to identify phosphopeptide-binding modules, said method comprising the steps of:

(a) providing an immobilized phosphopeptide library and an immobilized peptide library;

(b) contacting said libraries with a polypeptide or polypeptide fragment; and

(c) detecting preferential binding, wherein preferential binding to said phosphopeptide library in comparison to said peptide library identifies said polypeptide or polypeptide fragment as a phosphopeptide binding module.

21. (Withdrawn) A method to identify non-phosphopeptide-binding modules, said method comprising the steps of:

(a) providing an immobilized degenerate phosphopeptide library and an immobilized peptide library;

(b) contacting said libraries with a polypeptide or polypeptide fragment; and

(c) detecting preferential binding, wherein preferential binding to said peptide library in comparison to said phosphopeptide library identifies said polypeptide or polypeptide fragment as a non-phosphopeptide binding module.

22. (Withdrawn) A method to identify phosphopeptide-binding modules in the DNA damage response pathway, said method comprising the steps of:

(a) providing an immobilized pSer or pThr degenerate phosphopeptide library and an immobilized Ser or Thr peptide library;

(b) contacting said libraries with a polypeptide or polypeptide fragment; and

(c) detecting differential binding, wherein preferential binding to said

phosphopeptide library in comparison to said peptide library identifies said polypeptide or polypeptide fragment as a phosphopeptide binding module.

23. (Withdrawn) A degenerate phosphopeptide comprising a pSer or pThr that binds a tandem BRCT domain.

24. (Withdrawn) A phosphopeptide binding module comprising a BRCT tandem domain.

25. (Withdrawn) The phosphopeptide binding module of claim 23, wherein said BRCT tandem domain comprises at least 100 amino acids of the 3rd and 4th BRCT domains of PTIP.

26. (Cancelled)

27. (Withdrawn) The BRCT tandem domain of claim 24, wherein said tandem domain functions as a single module in phosphopeptide binding.

28. (Withdrawn) A complex comprising a tandem BRCT phosphopeptide binding module and a phosphopeptide comprising a pSer or pThr.

29. (Withdrawn) The complex of claim 28, wherein said tandem BRCT phosphopeptide binding module is a fragment of PTIP in complex with a phosphopeptide.

30. (Withdrawn) A method for identifying a candidate compound for the treatment or prevention of a neoplasia, said method comprising detecting binding of said phosphopeptide binding module to a phosphopeptide in the presence of said candidate

compound, wherein a candidate compound that modulates said binding is a compound useful for the treatment or prevention of a neoplasia.

31. (Withdrawn) The method of claim 30, wherein said phosphopeptide binding module is a tandem BRCT binding domain.

32. (Withdrawn) A method for identifying a peptidomimetic compound that modulates BRCT biological activity, said method comprising the steps of:

a) contacting the phosphopeptide of claim 30 and a BRCT binding domain domain polypeptide to form a complex between said phosphopeptide and said PBD;

b) contacting said complex with a candidate compound; and

c) measuring the displacement of said phosphopeptide from said BRCT binding domain, wherein said displacement of said phosphopeptide from said BRCT binding domain indicates that said candidate compound is a peptidomimetic compound that modulates BRCT binding domain biological activity.

33. (Withdrawn) A method for identifying a peptidomimetic compound that modulates BRCT binding domain biological activity, said method comprising the steps of:

a) contacting the phosphopeptide of claim 1 and a BRCT binding domain in the presence of a candidate compound; and

b) measuring binding of said phosphopeptide and said BRCT binding domain, wherein a reduction in the amount of binding relative to the amount of binding of said phosphopeptide and said polypeptide in the absence of said candidate compound indicates that said candidate compound is a peptidomimetic compound that modulates BRCT binding domain biological activity.

34. (Withdrawn) The method of claim 30, wherein said BRCT binding domain is selected from a group consisting of BRCA1 and PTIP.

35. (Withdrawn) A method to identify a peptide-binding module, said method comprising the steps of:

(a) providing an immobilized modified peptide library and an immobilized peptide library;

(b) contacting said libraries with a polypeptide or polypeptide fragment; and

(c) detecting preferential binding, wherein preferential binding to said modified peptide library in comparison to said peptide library identifies said polypeptide or polypeptide fragment as a modified peptide binding module.

36. (Withdrawn) A method for identifying a binding pair consisting of a modified peptide and a peptide-binding domain comprising the steps of:

a) providing a biased peptide library comprising a collection of modified peptides fixed to a solid support, each peptide having one amino acid residues whose position is invariant;

b) providing a pooled cDNA library, wherein the cDNA library is positioned for protein expression;

c) expressing the pooled cDNA library in the presence of a detectable label;

d) contacting the peptide library and the expressed cDNA library; and

e) detecting a modified peptide and peptide-binding domain interaction, wherein an interaction identifies a modified peptide and peptide-binding domain binding pair.

37. - 38. (Cancelled)

39. (Currently Amended) The computer of claim 1, said memory having stored

therein at least two sets of x, y, and z atomic coordinates from Table 5, or a mathematical modification of Table 5 that preserves the relative relationships among the coordinates of Table 5, ~~or surrogate coordinates thereof, from Table 5 for~~ from atoms of each of ~~the following~~ residues: His-538, Lys-540, Trp-414, and Leu-491 of a Polo-box domain of a Plk-1 Polo-like kinase or atomic coordinates that have a root mean square deviation of said coordinates less than 3 Å.

40. (Currently Amended) The computer of claim 39, said memory having stored therein at least three sets of x, y, and z atomic coordinates from Table 5, or a mathematical modification of Table 5 that preserves the relative relationships among the coordinates of Table 5, ~~or surrogate coordinates thereof, from Table 5 for~~ from atoms of each of ~~the following~~ residues: His-538, Lys-540, Trp-414, and Leu-491 of a Polo-box domain of a Plk-1 Polo-like kinase or atomic coordinates that have a root mean square deviation of said coordinates less than 3 Å.

41. (Currently Amended) The computer of claim 40, said memory having stored therein at least four sets of x, y, and z atomic coordinates from Table 5, or a mathematical modification of Table 5 that preserves the relative relationships among the coordinates of Table 5, ~~or surrogate coordinates thereof, from Table 5 for~~ from atoms of each of ~~the following~~ residues: His-538, Lys-540, Trp-414, and Leu-491 of a Polo-box domain of a Plk-1 Polo-like kinase or atomic coordinates that have a root mean square deviation of said coordinates less than 3 Å.

42. (Currently Amended) The computer of claim 41, said memory having stored therein at least five sets of x, y, and z atomic coordinates from Table 5, or a mathematical modification of Table 5 that preserves the relative relationships among the coordinates of Table 5, ~~or surrogate coordinates thereof, from Table 5 for~~ from atoms of each of ~~the~~

~~following~~ residues~~:~~ His-538, Lys-540, Trp-414, and Leu-491 of a Polo-box domain of a Plk-1 Polo-like kinase or atomic coordinates that have a root mean square deviation of said coordinates less than 3 Å.

43. (Currently Amended) The computer of claim 1, wherein said ~~coordinates have~~ ~~a~~ root mean square deviation is ~~of~~ less than 2 Å.

44. (Currently Amended) The computer of claim 43, wherein said ~~coordinates~~ ~~have a~~ root mean square deviation is ~~of~~ less than 1 Å.